REMARKS

Claims 1-12, 30, 45, 46, and 53-62 are pending in this application. Claims 58, 61, and 62 stand withdrawn as being directed to a non-elected invention. Claims 1-12, 30, 45, 46, 53-57, 59, and 60 are rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. Claims 1-12, 30, 45, 46, 53-57, 59, and 60 are provisionally rejected for obviousness-type double patenting over claims 1-14 and 35-49 of co-pending U.S. Patent Application No. 10/358,664. Finally, claims 1-12, 30, 45, 46, 53-57, 59, and 60 are rejected for obviousness-type double patenting over claims 1-15 of U.S. Patent No. 6,660,487 or claims 1-18 of U.S. Patent No. 6,599,710. By this reply, Applicant cancels claims 45 and 46, amends claims 1, 9, 30, and 59, and addresses each of the rejections.

Support for the Amendment

Support for the amendment is found on, e.g., page 21, line 3, page 22, line 6, and page 23, line 13, of the specification as filed, as well as in presently canceled claim 46. No new matter is added by the amendment.

Rejection under 35 U.S.C. § 112, first paragraph

Present claims 1-12, 30, 53-57, 59, and 60 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Office states:

> [T]he specification only discloses limited data obtained on NOD female mice wherein treatment with live splenocytes and CFA prolong survival of syngeneic islet graft and...[restores] normoglycemia (see examples 1-4 and Table 1 and 2 in particular)...[S]ince there is no animal model studies and data in the specification to show the effect[] of the claimed method for increasing or maintaining the number of any functional cells of any predetermined type of any organ or any tissue comprising administration to the subject a composition of enriched pluripotent cells that express Hox 11 gene alone or in combination with administering TNF-alpha or TNF-alpha agonist or TNF-alpha inducing substances, [it] is unpredictable how one skilled in the art can practice the invention without an undue amount of experimentation. (Office Action, pp. 3-5.)

The Office further states:

> Demonstrating prolonged survival of syngeneic islet graft restoration of normoglycemia in diabetic NOD mice...after administering live splenocytes and

> CFA cannot alone support the predictability of a method for increasing or maintaining the number of any functional cells of any predetermined type of any organ or tissue, by simply administering to a mammal a composition of enriched pluripotent cells that express the Hox 11 gene alone or in combination with administering TNF-alpha or TNF-alpha agonist or TNF-alpha inducing substance (Office Action, p. 4).

The Office relies on scientific publications, such as Atkinson et al. (hereafter "Atkinson"), for the proposition that experimental data generated using the NOD mouse model are not reasonably predictive of success in a human. The Office's characterization of Atkinson to discount the utility of the NOD mouse as a model of human type I diabetes is objectively incorrect.

Atkinson points out several considerations of which a practitioner (e.g., a scientist) should be aware when working with the NOD mouse model. Every animal model, including non-human primates, possesses inherent strengths and weaknesses when used to simulate a human condition (e.g., a disease). Accordingly, no animal model of a human condition can be considered perfect. Importantly, the Office fails to note or consider the explicit statements of Atkinson that the NOD mouse model, despite its deficiencies, has "enhanced our appreciation of the etiologic complexity of type 1 diabetes in humans and provides an example of how promising results obtained in an animal model can be translated into human clinical trials" (p. 604) or that the NOD mouse is "the favored model for investigations into the etiopathogenesis of autoimmune, T cell-mediated type 1 diabetes in humans" (p. 601). Thus, Atkinson plainly acknowledges the utility and favored status of the NOD mouse in modeling human type I diabetes; Atkinson does not suggest that the NOD mouse model cannot be used to predict success in treating human disease. The Office's statements to the contrary are factually inaccurate.

Furthermore, none of the publications cited by the Office raise doubts about whether the data presented in Applicant's specification, and in the Faustman declaration (submitted with the reply to Office Action on September 12, 2007), which demonstrate the restoration of pancreatic islet cells following the administration of *Hox11*-expressing splenocytes in an NOD mouse model, would be reasonably predictive of the successful treatment or stabilization of type I diabetes in a human. The M.P.E.P. § 2164.02 states:

> 'Correlation' as used herein refers to the relationship between in vitro or in vivo animal model assays and a disclosed or a claimed method of use. ...[T]he examiner must weigh the evidence for and against correlation and decide whether one skilled in the art would accept the model as reasonably correlating to the condition.

The perceived deficiencies of the NOD mouse (as discussed in Atkinson, and further in Kaufman et al.) and other, non-related animal models (as described in Feldman et al., Mestas et al., and Van Noort et al.) do not detract from the clear acknowledgement by Atkinson of the broad acceptance in the scientific community of the NOD mouse as a correlative model of human type I diabetes.

The Office has acknowledged that the instant claims are enabled "for a method of restoration of normoglycemia...in NOD mice" (Office Action, p. 3). By this reply, Applicant amends claim 1 to recite a human with an injured, damaged, or pancreatic islet cell deficient pancreas. Data generated using the NOD mouse model, in light of extrinsic evidence, e.g., Atkinson, as well as the specification and Faustman Declaration, render reasonably predictable the success of the presently claimed methods in a human. Furthermore, the specification must be taken as objectively enabled (M.P.E.P. § 2164.04); the Office has not provided any reason to doubt the objective truth of the specification. Present claims 1-12, 30, 53-57, 59, and 60 plainly satisfy the enablement requirement of 35 U.S.C. § 112 because Applicant's specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to their entire scope as presently amended (M.P.E.P. § 2164.02, *supra*).

Applicant respectfully requests that the rejection of present claims 1-12, 30, 53-57, 59, and 60 for lack of enablement be withdrawn.

Obviousness-Type Double-Patenting Rejection

Present claims 1-12, 30, 53-57, 59, and 60 are provisionally rejected for obviousness-type double patenting over claims 1-14 and 35-49 of co-pending U.S. Patent Application No. 10/358,664 (hereafter "the '664 application"). This rejection is in error and should be withdrawn. The claims of the '664 application do not teach or suggest a method of treating a human involving the administration to a human of "a composition enriched in pluripotent cells

that express the Hox11 gene." Thus, the subject matter of present claims 1-12, 30, 53-57, 59, and 60 is patentably distinct from the subject matter recited in the claims of the '664 application. The provisional obviousness-type double patenting rejection should be withdrawn.

Present claims 1-12, 30, 53-57, 59, and 60 also stand rejected for obviousness-type double patenting over claims 1-15 of U.S. Patent No. 6,660,487 (hereafter "the '487 patent") or claims 1-18 of U.S. Patent No. 6,599,710 (hereafter "the '710 patent"). This rejection is in error and should be withdrawn. The claims of the '487 and '710 patents do not teach or suggest a method of treating a human involving the administration to a human of "a composition enriched in pluripotent cells that express the Hox11 gene." Thus, the subject matter of present claims 1-12, 30, 53-57, 59, and 60 is patentably distinct from the subject matter recited in the claims of the '487 and '710 patents. The obviousness-type double patenting rejection should be withdrawn.

CONCLUSION

Applicant submits that present claims 1-12, 30, 53-57, 59, and 60 are in condition for allowance, and such action is respectfully requested.

Enclosed is a Request for Continued Examination as well as a petition to extend the period for replying for three months, to and including July 24, 2008, and a check for the fees required under 37 C.F.R. § 1.17(a) and 1.17(e).

If there are any other charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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